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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,761	02/21/2006	Takamasa Watanabe	0020-5502PUS1	6669
2292	7590	12/03/2007		
BIRCH STEWART KOLASCH & BIRCH			EXAMINER	
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			ART UNIT	PAPER NUMBER
			1644	
			NOTIFICATION DATE	DELIVERY MODE
			12/03/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/568,761	WATANABE ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Maher M. Haddad	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 12 September 2007.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 19-30 is/are pending in the application.
- 4a) Of the above claim(s) 21-30 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 19 and 20 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>2/21/06, 9/6/06 &amp; 10/30/07</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|   | 6) <input type="checkbox"/> Other: _____                          |

DETAILED ACTION

1. Claims 19-30 are pending.
2. Applicant's election without traverse of Group I, claims 19-20 directed to a method for preventing, improving or treating of inflammatory bowel disease (IBD), comprising administering a therapeutic agent comprising an effective amount of anti-CD81 antibody to a mammal in need thereof, filed on 9/12/07, is acknowledged.
3. Claims 21-30 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.
4. Claims 19-20 are under examination as they read on a method for preventing, improving or treating of inflammatory bowel disease (IBD), comprising administering a therapeutic agent comprising an effective amount of anti-CD81 antibody to a mammal in need thereof.
5. Applicant's IDS, filed 2/21/06, 9/6/06 and 10/31/07, is acknowledged, however, references BB, BC, BD and BF were considered only in regard to the English Abstract as the entire English documents were not found.
6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Page 12, 1<sup>st</sup> Full ¶ and page 13, 3<sup>rd</sup> ¶ contain embedded hyperlinks and/or other forms of browser-executable code, which are impermissible and require deletion.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:  
*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*
8. Claims 19-20 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of improving or treating IBD comprising administering the anti-CD81 monoclonal antibody 2F7 (once the deposit is satisfy), does not reasonably provide enablement for a method for "preventing" improving or treating of inflammatory bowel disease (IBD), comprising administering a therapeutic agent comprising an effective amount of "anti-CD81 antibody" to a mammal in need thereof in claim 19, wherein the anti-CD81 antibody is a

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monoclonal antibody in claim 20. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The nature of the invention is such that it would require the administration of anti-CD81 antibody that would prevent/improve/treat a mammalian subject with IBD. The specification, under example 5, page 99 discloses that the pharmacological effects of an anti-CD81 antibody to TNBS-induced mouse colitis models. The exemplification is drawn to the improve symptom of colitis (S.D) and improve shortening of the intestinal length to demonstrate the ability of the anti-CD81 antibody improve or treat the colitis in an assay that recapitulates the SSZ administration.

Claim 19 recites any anti-CD81 antibodies. The specification under 32¶ discloses that the "anti-CD81 antibody" in the specification includes an antibody which specifically recognizes CD81. Specifically, it includes an antibody capable of specifically recognizing an expression product (protein) of the CD81 gene. However, Levy et al (Annu Rev Immunol. 1998;16:89-109) teach that CD81 is involved in a broad range of cellular functions, as revealed by the binding of mAbs. Whether the antibodies evoke their effect by mimicking a natural ligand or by altering the interactions between CD81 and its associated proteins is unknown. While the molecule is expressed on most cells, some of the antibody-triggered effects can be seen only in a subset of cells. Also, some cellular responses are mAb-dependent, sine mAbs reacting with different CD81 epitopes do not elicit the same response in a given cell line (see page 100, 2<sup>nd</sup> ¶). For example, mAb 5A6 has the ability to inhibit proliferation of a B lymphoma cell line. Further testing indicated that additional B cell lines were sensitive to the antiproliferative effect of the antibody and that most T cells were insensitive (see page 100, 3<sup>rd</sup> ¶). Further, two different anti-CD81 mAbs, 5A6 and ID6, are strong inducer of homotypic adhesion in hematolymphoid cells. Both B and T cells are comparably induced to aggregate by these antibodies. The other anti-CD81 mAbs from the fifth international Leukocyte Workshop were less potent in inducing adhesion. The mAbs JS81 and 4TM-2 induced an intermediate response, whereas JS64 and 4TM-1 induced a minimal response (see page 101 Under Adhesion). In adhesion to inducing adhesion, the anti-CD81 mAb JKT.1 changed the morphology of CD166Tcells, where the immobilized antibody induced the formation of processes by the cell (see page 102, under Change in Cell Morphology). The anti-CD81 mAb, M38, was found by its ability to inhibit

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HTLV-induced syncytium formation (see page 102 under Inhibition of Syncytium Formation). Finally, the mAb 5A6 and 1D6 increase TNF- $\alpha$  production in J.Y and EBV-positive cell line (see page 103 under Release of TNF- $\alpha$ ). Given that mAbs reacting with different CD81 epitope do not elicit the same response in a given cell line, it is unpredictability as to which antibody would treat IBD. Without detailed direction as to which anti-CD81 antibody are essential for the treatment of IBD, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of anti-CD81 antibodies encompassed by the instant claims would share the ability to treat IBD, other than the anti-CD81 antibody, 2F7 used in example 5 to improve symptoms of colitis and improve shortening of the intestinal length (see page 100, 2<sup>nd</sup> full ¶). The skilled in the art would not wish to increase the production of TNF- $\alpha$  or induce adhesion in treating IBD.

Further, at issue is whether or not the claimed anti-CD81 antibody would function to "prevent" IBD. The specification under Example 5 discloses 2F7 mAbs improved symptoms of colitis and intestinal length shortening (see Table 3, Pg. 102 in particular). No anti-CD81 antibody was administered to the mice before the TNBS treatment to demonstrate any prevention of colitis. Further, the specification fails to provide guidance as to how to totally prevent (100% prevention) IBD. The specification does not provide sufficient guidance on how to sufficiently prevent the occurrence of IBD.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claim 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S Pat. No. 6,423,501.

The '501 patent teaches a method of treating inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which induces CD81-mediated signal transduction. For example, the method can be used to treat inflammatory responses associated with disorders such inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) (see col., 13, lines 34-45 in particular). The '501 patent teaches that agents described herein can be anything which binds to or interacts with CD81 and induces (i.e., activates) or enhances CD81-mediated signal transduction. For example, the agent can be a polyclonal or monoclonal antibody, such as an anti-CD81 antibody. In particular embodiments, the antibody is 5D1 or 1A12 (see col., 9, line 65 to col., 10, line 3 in particular).

The reference teachings anticipate the claimed invention.

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11. Claim 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/25647 (IDS ref. No. BJ).

The '647 publication teaches a method of treating inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which induces CD81-mediated signal transduction. For example, the method can be used to treat inflammatory responses associated with disorders such inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) (see col., 26, lines 12-22 in particular). The '501 patent teaches that agents described herein can be anything which binds to or interacts with CD81 and induces (i.e., activates) or enhances CD81-mediated signal transduction. For example, the agent can be a polyclonal or monoclonal antibody, such as an anti-CD81 antibody. In particular embodiments, the antibody is 5D1 or 1A12 (see Pg. 19, line 3-9 in particular).

The reference teachings anticipate the claimed invention.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 5, 2007



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